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10/018,616	06/10/2002	Roger N. Brummel	A0000060-01-DRK	7778

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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	6

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/018,616	Applicant(s) BRUMMEL ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. Applicants' claim for benefit of US Provisional Application No. 60/142215 filed on 07/02/1999 under 35 U.S.C. 119(e) is acknowledged. Also, applicants' claim for domestic priority under 35 U.S.C Section 120 and/or 121 is acknowledged.

Drawings

2. The drawings filed on 06/10/2002 are accepted by the Examiner.

Information Disclosure Statement

3. Acknowledgement is made of applicant's submitting of the information disclosure statement (IDS) on December 17, 2001.

4. With respect to DE 19802327 A1 in the submitted PTO-1449, although Applicants checked box with translation, no translation has been provided to the Office. The information disclosure statement filed December 17, 2001 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

5. With respect to "PCT International Search Report, PCT/US00/17039" in the submitted PTO-1449, the information disclosure statement filed December 17, 2001 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information

submitted for consideration by the Office. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 5 is rejected under 35 USC 112, first paragraph, because the specification while being enabling for "a composition comprising gabapentin and pregabalin with a ratio of gabapentin to pregabalin from 1:1 to 250:1 by weight", does not reasonably provide enablement for "a pharmaceutical composition with a ratio from 1:1 to 250:1 by weight". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

In view of the specification, the critical feature of the instant invention is related to a composition comprising combination of gabapetin and pregabalin. However, the instant claim fails to recite such feature which is taught as critical in the specification. Applicants' omission of such essential feature in the claim would not allow the skilled artisan to make the full scope of the instantly claimed invention that are directed to vast number of possible compositions having the ratio from 1:1 to 250:1 by weight. The specification provides inadequate direction or guidance regarding how to make the instantly claimed composition other than the composition comprising combination of gabapentin and pregabalin in the range of the specific ratio. In absence of providing the active ingredients of the composition in the claim, the skill artisan would have to carry out burdensome experiment as well as an exhaustive search for the embodiments suitable to practice the claimed invention. In view of the state of the prior art, high level of ordinary skill in the pharmaceutical art, high level of unpredictability in the pharmaceutical art, the limited numbers of working examples in the specification and the breadth of claims, it would take undue trials and errors to practice the claimed invention.

As stated above, the claim which omits matter disclosed to be essential to the invention as described in the specification can be rejected under 35 USC 112, first paragraph, as not enabling. See MPEP § 2172.01 and 2164.08(c).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 further limits the claimed 1 composition by reciting "gabapentin is in a ratio from 1:1000 and pregabalin is from 1:1000".

The instant specification discloses that the claimed composition contains a ratio of about 1:1 to about 1000:1; preferably 1:1 to 500:1 and particularly from 1:1 to 250:1 parts by weight of gabapentin or a pharmaceutically acceptable salt or hydrate thereof to pregarbalin or a pharmaceutically acceptable salt or hydrate thereof (page 9, lines 11-14). It appears in view of the instant specification that the ratio of gabapentin to pregabalin in said composition is from about 1:1 to about 1000:1, preferably 1:1 to about 500:1, more preferably 1:1 to 250:1. For instance, when 250 parts of gabapentin is used, 1 part of pregarbalin should be used in the instant invention. However, applicants' recitation of "gabapentin is in a ratio from 1:1000 and pregabalin is from 1:1000" makes the claimed invention unclear and vague and leaves the reader in doubt as to the meaning of the claimed invention. It is not clear whether (i) the claimed ratio refers to the dosage amounts of gabapentin in relation to pregabalin or (ii) the dosage amount of gabapentin or pregabalin in relation to any other unspecified ingredients. In this regard, it is considered that the meaning of the claim should be clear from the wording of the claim alone.

For the examination purpose, "gabapentin is in a ratio from 1:1000 and pregabalin is from 1:1000" is interpreted as "gabapentin to pregabalin is in a ratio from 1:1 to 1000:1".

8. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP

§ 2172.01. The omitted elements are: gabapentin and pregabalin. It appears in view of the instant specification that the essential feature of the claimed invention is a synergistic combination of gabapentin and pregabalin. However, applicants' omission of such essential feature in claim 5 renders the claimed invention vague and indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Kompis et al. (US 5721242).

The claim invention is drawn to a composition wherein a ratio from 1:1 to 250:1 by weight.

Kompis discloses a antibiotic composition comprising epiroprim and dapsone wherein the ratio of epiroprim to dapsone is in the ratio of about 1:1 to about 2:1 parts by weight (claim 3).

Since the instant claim read on any composition containing any components wherein said composition has "a ratio from 1:1 to 250:1 by weight", the referenced composition clearly anticipates the instantly claimed invention.

10. Claims 1-2, 6-7 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Hurtt et al. (US 6,451,857 B1).

The claims 1-2 are drawn to a composition comprising gabapentin and pregabalin wherein claim 2 requires gabapentin and pregabalin "in the form of the free acid". The claims 6-7 and 9 are drawn to a method for the treatment of pain with said composition wherein claim 6 requires "unit dosage form"; claim 7 requires "concomitant administration" of gabapentin and pregabalin; and claim 9 requires "hyperalgesia, allodynia and inflammatory".

With respect to claims 1-2, 6 and 9,

Hurtt teaches a composition comprising two or more anti-epileptic compounds combined with one or more compounds selected from NSAID, analgesic, NMDA receptor antagonists, or combinations thereof, namely gabapentin/pregabalin/opioid, gabapentin/pregabalin/NSAID, gabapentin/pregabalin/naproxen (column 5, lines 38-49), that is useful for treating pain including inflammatory pain (column 5, lines 50-60 and column 6, lines 8-19) wherein said composition is prepared in unit dosage form (column 6, lines 20-45).

Since the instant claims allow for the inclusion of any other unspecified ingredients in the composition by reciting open transitional language such as "comprises", the referenced composition anticipates the claimed invention.

Although Hurtt is silent about "synergistic effect" in independent claim 1, such preamble to the claim is not limiting to the interpretation of the composition. Thus, the referenced composition anticipates the claimed invention.

Although Hurtt is silent about the presence of gabapentin and pregabalin "in the form of the free acid", the referenced gabapentin and pregabalin in said composition must be inherently presented in the composition "in the form of the free acid" since the referenced gabapentin and pregabalin in Hurtt are used in the form of compound, not in salt forms. Therefore, the reference anticipates the claimed invention.

With respect to claim 7,

Hurtt also teaches the claimed method for treating pain by the co-administration of said composition (column 2, lines 41-52 and column 6, lines 1-7).

Since the referenced co-administration "metes and bounds" the claimed "concomitant administration", the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 3, 4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hurtt et al (US 6,451,857 B1).

The teaching of Hurtt'857 has been discussed in above 35 USC 102(e) rejection.

The teaching of Hurtt'857 differs from the claimed invention in the specific range of ratio of gabapentin to pregarbalin or the specific range of dosage amount of gabapentin and pregabalin in the composition wherein claims 3-4 require the ratio of gabapentin to pregabalin " from 1:1 to 1000:1" by weight and claim 8 requires "gabapentin is administered in the amount of from 5 to 250mg and pregabalin in the amount of from 5 to 25mg". However, the determination of a

dosage or ratio having the optimum therapeutic is well within the skill of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the drug. Those of ordinary skill in the art will readily optimize effective dosages or ratios as determined by good medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation.

Conclusion

12. No Claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon